IN THE CLAIMS

This listing of claims replaces all prior versions, and listings, in this application.

1. (currently amended) A modified bacterial surface layer (S-layer) protein, the modification comprising the internal insertion of a heterologous polypeptide, wherein said modified protein is able to crystallize.

2. (currently amended) [[The]] A protein according to claim 1, wherein:

(a) the unmodified protein is from a Gram-positive or non-aquatic bacteria~~, optionally a lactic acid bacteria or *Lactobacillus*~~; and/or

(b) the heterologous polypeptide is a functional polypeptide or a polypeptide of interest~~, optionally a binding or targeting protein (such as an antigen, antibody, or part thereof)~~.

3. (currently amended) A protein according to claim 1, wherein:

(c) the protein retains most of the full length sequence of the unmodified S-layer protein;

(d) the polypeptide is inserted at an internal location at least five amino acids from the C- or N-terminus; and/or

(e) the modified protein has a size of from 40 to 300 [[70]] kDa.

4. (currently amended) A protein according to claim 1 which:

(f) has a crystallization or ~~crystallisation or C-terminal~~ N-terminal domain that is predominantly basic, or hydrophobic; [[,]]

(g) an ~~N-terminal~~ C-terminal domain which is ~~either~~ predominantly hydrophilic; or

(h) has alternating hydrophobic and hydrophilic regions.

5. (currently amended) A protein according to claim 1, wherein the heterologous polypeptide is inserted at a location in the protein ~~either~~ so that it is:

(i) exposed, or present on the cell surface;

(j) present in the surface layer, or the cell wall; or

(k) is protected from external proteolytic processing or is not recognised or bound by external antibodies.

6. (currently amended) A protein according to claim 1, wherein the modified or unmodified protein:

(l) crystallizes ~~crystallises, optionally~~ into an oblique lattice ~~(such as of p1 or p2 symmetry)~~;

(m) has a cell wall anchor domain;

(n) has a pI of at least 7; and/or

(o) is predominantly basic.

7. (currently amended) A protein according to claim 1, wherein the polypeptide comprises an antigen causing or specific for a disease~~, and optionally is an antigen recognisable by an antibody or is all or part of an antigen from an anaerobic bacteria, optionally *Clostridium*~~.

8. (currently amended) A protein according to claim 1 which [[(]]in unmodified form[[)]] is from *Lactobacillus acidophilus*, *L. crispatus*, *L. helveticus*, *L. amylovorus*, or *L. gallinarum*.

9. (currently amended) A fragment of a ~~bacterial surface layer (S-layer)~~ protein according to claim 1 which is:

a) an N-terminal fragment or a fragment that is capable of forming a dimer with ~~an other~~ another such fragment or a trimer with two other such fragments;

b) capable of forming dimers with another such fragment and either

(i) includes an immunodominant or exposed loop region and is from 20 to 200 amino acids long; or

(ii) excludes an entire immunodominant or exposed loop region and is from 20 to 155 amino acids long.

10. (previously presented) A polynucleotide encoding a protein according to claim 1.

11. (original) A vector comprising a polynucleotide according to claim 10.

12. (currently amended) A host cell comprising, or which [[is]] has been transformed with a vector according to claim 11.

13. (currently amended) A bacteria expressing a bacterial surface layer (S-layer) protein ~~(or fragment)~~ according to claim 1 or a fragment thereof ~~of a bacterial surface layer (S-layer) protein~~ which is:

a) an N-terminal fragment or a fragment that is capable of forming a dimer with ~~an other~~ another such fragment or a trimer with two other such fragments;

b) capable of forming dimers with another such fragment and either

   (i) includes an immunodominant or exposed loop region and is from 20 to 200 amino acids long; or

   (ii) excludes an entire immunodominant loop region and is from 20 to 155 amino acids long.

14. (currently amended) A bacteria according to claim 13 which is a lactic acid bacteria~~, optionally from *Lactobacillus*, and is preferably *L. plantarum*, *L. acidophilus* or *L. casei*~~.

15. (currently amended) A modified bacteria [[(]]other than *L. casei* or *Bacillus*[[)]] which has been modified to express a heterologous surface layer (S-layer) protein, wherein said heterologous surface layer (S-layer) protein is a modified bacterial surface layer (S-layer protein according to claim 1.

16. (original) A bacteria according to claim 15 which would not normally, or as a wild-type or in unmodified form does not, possess a surface layer.

17. (previously presented) A modified bacteria according to claim 15 which is a *Lactobacillus* cell and/or the S-layer has its own, original, cell wall anchor.

18. (currently amended) A bacteria according to claim 15 which is a *Lactobacillus* bacterial cell~~, such as *L. casei*~~, and/or the S-layer protein is from *Lactobacillus* bacteria~~, such as *L. acidophilus*~~.

Claims 19-20 (canceled)

21. (currently amended) A modified bacteria expressing only, or homogeneously, a ~~heterologous or~~ modified surface layer (S-layer) protein according to claim 1.

22. (currently amended) A bacteria according to claim 21 having a genome which includes a polynucleotide encoding a ~~heterologous~~ modified S-layer protein, ~~optionally integrated into the genome,~~ and/or where the polynucleotide encoding the normal or wild-type S-layer protein has been silenced, replaced, switched off or otherwise rendered non-expressed.

23. (currently amended) A bacteria according to claim 22, wherein the ~~heterologous or~~ modified S-layer protein is the sole or only S-layer protein expressed by the bacterial cell and/or the cell does not express any wild-type S-layer protein.

24. (currently amended) A bacteria according to claim 22, wherein the S-layer protein is located on the surface of the cell wall and/or a multiplicity of S-layer proteins form an S-layer.

25. (currently amended) A vaccine comprising a bacteria according to claim 13, a modified bacteria ~~(other than *L. casei* or *Bacillus*)~~ which has been modified to express a heterologous surface layer (S-layer) protein, wherein said heterologous surface layer (S-layer) protein is a modified bacterial surface layer (S-layer) protein ~~an *L. casei*~~

~~bacterial cell expressing a bacterial surface layer (S-layer) protein that is either not from *L. crispatus* or is not a collagen binding protein~~ or a modified bacteria expressing only, or homogeneously, a ~~heterologous or~~ modified surface layer (S-layer) protein, wherein said bacteria has GRAS (generally regarded as safe) status.

26. (original) A vaccine according to claim 25 which is an oral or nasal vaccine and/or additionally comprises an adjuvant.

27. (currently amended) A sheet or ~~(optionally crystalline)~~ monolayer or 2-dimensional array comprising a plurality of bacterial surface layer proteins, at least one of which is modified protein according to claim 1.

28. (original) A solid surface, liquid-air interface, lipid film, liposome or solution comprising a sheet, monolayer or array according to claim 27.

29. (original) A solid surface according to claim 28 to which is bound one or more (macro) molecules, such as an enzyme, antibody or other binding molecule, receptor, antigen or ligand.

30. (previously presented) A solid surface comprising a layer of S-proteins, at least a plurality of which are modified proteins according to claim 1, sandwiched between the surface and a layer of functional molecules.

31. (currently amended) A sensor, molecular sieve or ion trap comprising a sheet, layer or array according to claim 27 or a surface comprising said [[a]] sheet, monolayer or array ~~according to claim 27~~.

32. (previously presented) A sensor, molecular sieve or ion trap comprising a solid surface comprising a layer of S-proteins, at least a plurality of which are modified

proteins according to claim 1, sandwiched between the surface and a layer of functional molecules.

33. (new) A protein according to claim 1, wherein said modified protein is able to form a sheet, crystalline monolayer or two-dimensional array.

34. (new) A protein according to claim 8, wherein the unmodified protein is from *Lactobacillus acidophilus* and wherein the heterologous polypeptide is inserted at a location from amino acid 1 to amino acid 290 of SEQ ID NO:2.

35. (new) A protein according to claim 34, wherein the heterologous polypeptide is inserted at a location:

(i) from amino acid 1 to amino acid 20 of SEQ ID NO:2;
(ii) from amino acid 35 to amino acid 55 of SEQ ID NO:2;
(iii) from amino acid 100 to amino acid 130 of SEQ ID NO:2; and/or
(iv) from amino acid 110 to amino acid 140 of SEQ ID NO:2.

36. (new) A protein according to claim 35, wherein the heterologous polypeptide is inserted at a location:

(i) from amino acid 5 to amino acid 10 of SEQ ID NO:2;
(ii) from amino acid 40 to amino acid 50 of SEQ ID NO:2;
(iii) from amino acid 110 to amino acid 120 of SEQ ID NO:2; and/or
(iv) from amino acid 120 to amino acid 130 of SEQ ID NO:2.

37. (new) A protein according to claim 36, wherein the position where the heterologous polypeptide is inserted at amino acid 7, 45, 114 and/or 125 of SEQ ID NO:2.

38. (new) A method of using a protein according to claim 1, said method comprising administering the modified protein or a bacteria expressing the modified protein to a human or animal by mucosal, nasal, oral, or vaginal delivery.

39. (new) A method of making a protein according to claim 1, said method comprising cultivating a host cell under conditions to provide for expression of the protein and recovering the expressed protein.